Type 2 innate lymphoid cell activation by CysLTs

Taylor Doherty, M.D.
UC San Diego

**Background**
- Type 2 innate lymphoid cells (ILC2)
- ILC2 activation by *Alternaria alternata*

**Role of CysLT1R on mouse ILC2**
- Expression
- Th2 cytokine production and proliferation

**Human peripheral blood ILC2**
- PGD2-induced chemotaxis
- Allergen challenge in allergic rhinitis

**Type 2 innate lymphoid cells (ILC2)**

- ILC2 are lineage-negative lymphocytes (negative for B, T, NK, NKT and other known lineage markers) that produce IL-5 and IL-13 in response to IL-25, IL-33, and TSLP
Alternaria induces an innate type-2 response in the airways of unsensitized mice.

Lung ILC2 produce IL-5 and IL-13 after Alternaria challenge.

Lung ILC2 are absent in IL-7R deficient mice that are resistant to Alternaria-induced eosinophilia.

Role of CysLT1R on mouse lung ILC2.

Alternaria-induced innate eosinophilic response is dependent on bone marrow derived STAT6.
CysLT1R is expressed on lung and bone marrow ILC2 in mice

LTD4 induces CysLT1R-dependent ILC2 IL-5 and IL-13 production in vitro

LTD4 induces CysLT1R-dependent ILC2 IL-4 production and calcium influx in vitro

LTD4 induces ILC2 IL-5 production in WT mice in vivo partly dependent on CysLT1R

LTD4 potentiates Alternaria-induced ILC2 accumulation and proliferation

LTD4 promotes IL-5 producing ILC2 and airway eosinophilia during Alternaria challenges
Summary of Mouse CysLT1R Studies

- Lung and bone marrow mouse ILC2 express CysLT1R
- LTD4 induces ILC2 calcium influx and Th2 cytokine production (including IL-4) dependent on CysLT1R
- LTD4 induces ILC2 IL-5 production in-vivo, dependent on CysLT1R
- LTD4 potentiates accumulation and proliferation of lung ILC2 independent of adaptive immunity during Alternaria challenges

Human Peripheral Blood ILC2

Prostaglandin D2 regulates human type 2 innate lymphoid cell chemotaxis

Allergen challenge increases peripheral blood ILC2 in allergic rhinitis

Acknowledgements

- David Broide (UCSD)
- Jinny Chang, David Scott (Scripps)
- Hannah Walford, Naseem Khorram, Sean Lund, Rachel Baum (UCSD)
- Amit Mehta & Michael Croft (LIAI)
- Frank Austen, Joshua Boyce, Nora Barrett (Brigham & Women’s)
- Funding: NIH, ALA, AAAAI